REMARKS

Attached hereto is a marked-up version of the changes made to the specification. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Respectfully submitted,

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By _____

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Paragraph beginning on line 18 of page 9 has been amended as follows:

The amino acid sequence of calgranulin A is shown by [Sequence ID No. 1] (SEQ ID NOS 1 and 3) of the Sequence Table (Nature (1987) 330 (5) 80-82), and the amino acid sequence of calgranulin B is shown by [Sequence ID No. 2] (SEQ ID NOS 2 and 4) of the Sequence Table (the same source). Therefore, calgranulins including at least one of the following peptides can be given as preferable active form of calgranulins of the present invention.

Paragraph beginning on line 25 of page 9 has been amended as follows:

(i) A peptide consisting of the amino acid sequence 1-93 of [Sequence ID No. 1] (SEQ ID NOS 1 and 3) of the Sequence Table and binding calcium thereto.

Paragraph beginning at line 1 of page 10 has been amended as follows:

(ii) A peptide consisting of the amino acid sequence 1-114 of [Sequence ID No. 2] (SEQ ID NOS 2 and 4) of the Sequence Table and binding calcium thereto.

Paragraph beginning at line 4 of page 10 has been amended as follows:

(iii) A peptide having an amino acid sequence in which one or more amino acids are deleted from or added to the amino acid sequence of [Sequence ID No. 1 or 2] (SEQ ID NOS 3 or 4) of

the Sequence Table, or one or more amino acids in the amino acid sequence of [Sequence ID No. 1 or 2] (SEQ ID NOS 3 or 4) are replaced with other amino acids, binding calcium thereto, and exhibiting the activity of increasing secretion of granules of cell lines having granule secretion capability.

Paragraph beginning at line 5 of page 16 has been amended as follows:

As a method of causing calgranulin to over-expression, a method of recombining a gene encoding calgranulin in a known plasmid vector or virus vector, and introducing the recombinant into the cells can be given. The base sequence shown as [Sequence ID No. 1 or No. 2] (SEQ ID NOS 1 or 2) in the sequence table, for example, can be used as a gene encoding calgranulin. The recombinant vector can be introduced into the cells by the calcium phosphate method, the DEAE dextran method, lipofectin method, electric pulse method, or the like. The above-described various methods may be preferably used for introducing a calgranulin gene in a cell line and causing the calgranulin to over-expression. The cells are converted to cells having the above-mentioned permeabilized cell membrane and a water-soluble calcium compound is preferably introduced in the cell line. Specifically, a calgranulin gene is introduced into cells by incubating a plasmid vector or virus vector in which the calgranulin gene has been incorporated in the amount of the 1-200 _g per 0.5×10^7 to 3×10^7 cells at 4-40°C for 5-120 minutes together with 1-100 _g of calcium phosphate, 0.1-10 mg of DEAE dextran, or 1-100 _g of lipofectin, or by treating the plasmid vector or virus vector in which the calgranulin gene has been incorporated

in the amount of the 1-200 _g per $0.5x10^7$ to $3x10^7$ cells using a short electric pulse at 4-40°C for 1-30 minutes. The above-mentioned various methods may be used for introducing the water-soluble calcium compound.

Paragraph beginning on line 1 of page 19 has been amended as follows:

A calgranulin anti-sense gene can be obtained by inserting a gene having a base sequence complementary to the base sequence shown by [Sequence ID No. 1 or No. 2] (SEQ ID NOS 1 or 2), for example. In the present invention, a plasmid vector or virus vector is prepared by inserting 1-200 _g of this calgranulin anti-sense gene per $0.5x10^7$ to $3x10^7$ cells. The resulting vector is incubated at 4-40°C for 5-120 minutes with the addition of 1-100 _g of calcium phosphate, 0.1-10 mg of DEAE dextran, or 1-100 _g of lipofectin. Alternatively, a plasmid vector or virus vector with 1-200 _g of the calgranulin anti-sense gene inserted per $0.5x10^7$ to $3x10^7$ cells is added and treated by a short electric pulse at 0.05-0.5 kV at a temperature of 4-40°C for 1-30 minutes.